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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,443	02/22/2002	Mark Ray Alvis	437252001200	6302

25226 7590 10/20/2004

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,443	ALVIS ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-114* is/are pending in the application.

4a) Of the above claim(s) *11-17 and 42-114* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 18-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/3/04 and 7/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO IDS, RESPONSE TO RESTRICTION REQUIREMENT AND STATUS OF THE CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 3/3/04 and 7/8/04 and the response to the restriction requirement filed 7/8/04 are acknowledged, entered and considered. Claims 1-114 are now pending in the application.

ELECTION WITHOUT TRAVERSE

2. Applicant's election of Group I, species I (anesthetics) and subspecies A (bupivacaine) claims 1-10 and 18-41 in the communication filed 7/8/04 is acknowledged. Applicant has elected to prosecute the invention of Group I, species I and subspecies A (claims 1-10 and 18-41) without traverse and requested Group II, species and subspecies (upon allowance of a generic claim) (i.e., claims 42-113) be rejoined in accordance with the provisions of MPEP § 821.04 when the pending claims are found allowable. However, since all the pending claims are not allowed, claims 41-114 are withdrawn as non-elected invention. Hence, the Office action is directed to the merits of claims 1-10 and 18-41 (Group I, species I and subspecies A) as *per* elected invention.

OBJECTION TO THE ABSTRACT

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. The use of the phrase "e.g.," (for example) should be avoided because it is unclear whether the limitation(s) following the phrase is/are part of the disclosed invention. Thus, appropriate correction is required. See MPEP 608.01(b).

OBJECTION TO TRADEMARKS AND THEIR USE

4. The use of the trademarks "Zyderm®" and "Chirocaine®" have been noted in this application. The trademarks have not been capitalized, they should be capitalized wherever they appear and be accompanied by the generic terminology. Although, the use of trademarks are permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in a manner, which might adversely affect their validity as trademarks.

Further, the specification, which specifies the generic terminology should include, published product information sufficient to show that the generic terminology or the generic description are inherent in the article referred by the trademarks. These description requirements are made because the nature and composition of articles denoted by trademarks can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 7, 18-26, 30, 31 and 33-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 33 are indefinite in the recitation "wherein the collagen contains…..". Amendment of the claims to recite "wherein the collagen further contains……." Is suggested.

Claims 18-22 and 34-38 recite the limitation "the concentration" in line 1. There is insufficient antecedent basis for this limitation in claim 1 or claims 18-22 or claim 27 or claims 34-38, respectively.

Claims 23 and 39 are indefinite in the recitation "the total amount of pharmaceutical agent" because there is no proper antecedent basis "for the total amount " in claim 1 or claim 27. Claims 1 and 27 recite "an effective amount". Appropriate correction is required.

Similarly, claims 24, 25 and 40 are indefinite in the recitation "the amount of pharmaceutical agent" because there is no proper antecedent basis "for the amount " in claim 1 or claim 27. Claims 1 and 27 recite "an effective amount". Appropriate correction is required.

The syntax of claim 26 is indefinite and vague in the recitation "The composition of any of claims 1, further including one or more pharmaceutical acceptable excipient(s)" because there is only one claim1. Amendment of the claim to recite " The composition of claim 1, further comprising one or more pharmaceutically acceptable excipients" is suggested.

Claims 30 and 31 recite the limitation "the ratio" in line 1. There is insufficient antecedent basis for this limitation in claim 27 or claim 30 or claim 31.

Claim 41 is indefinite in the recitation "further including....". Amendment of the claim to recite "further comprising....." is suggested.

CLAIMS REJECTION-35 U.S.C. § 102(b)

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 8-10 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Pavelka et al., Poster No. 137 of "Safety Following Intra-articular Injection of Neu Visc™--Two Studies" Fourth World Congress of the Oslo Arthritis Research Society International, Vienna, Austria, total pages 2, September 1999.

The poster of Pavelka et al teaches the use of a formulation/composition comprising a commercially available Neu Visc™, a viscoelastic dispersion of Type I of highly purified fibrillar atelopeptide collagen containing or including 0.3% anesthetics such as lidocaine for reducing pain in osteoarthritis patients. With respect to the limitations of controlled release formulation of at least 48 hours or at least 72 hours, these limitations are considered as functional limitations which is inherent in a composition claim, as such no probative weight is given to the claimed

formulation/composition claim because the reference clearly teaches the use of the same composition for the same purposes of treating articular or incisional pain. Thus, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 1-3, 8-10 and 26 as drafted.

CLAIM REJECTIONS-35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 and 18-41 rejected under 35 U.S.C. 103(a) as being unpatentable over Pavelka et al., Poster No. 137 of "Safety Following Intra-articular Injection of Neu Visc™--Two Studies" Fourth World Congress of the Oslo Arthritis Research Society International, Vienna, Austria, total pages 2, September 1999 taken with Yamahira et al (U.S. Patent No. 4,855,134), Maeda et al (Journal of Controlled Release, Vol. 62, pp. 313-324, 1999), Batyrov et al (Stomatologiya, Vol. 61, No. 2, pp. 7-10, March-April, 1982, English Abstract) and Solanki et al (Arthroscopy, Vol. 8, No. 1, pp. 44-47, 1992).

The primary reference of Pavelka et al teaches as discussed above the use of a formulation/composition comprising a commercially available Neu Visc™, a viscoelastic dispersion of Type I of highly purified fibrillar atelopeptide collagen containing or

including 0.3% anesthetics such as lidocaine for reducing pain in osteoarthritis patients (See the whole reference) as directed to claims 1-3, 8-10 and 26. The prior art differs from claims 1-10 and 18-41 in not teaching a) the duration time of controlled release formulation, b) the ratio of collagen to pharmaceutical agent, c) the amount or the percentages of type I collagen, d) the concentration of the collagen and the pharmaceutical agent, and e) the use of anesthetics which is bupivacaine. With respect to the limitations of the duration time of controlled release formulation of at least 48 hours or at least 72 hours, these limitations are considered as functional limitations which is an expected characteristics of a composition claim, as such no probative weight is given to the claimed formulation/composition claim because the primary reference of Pavelka et al clearly teaches the use of the same composition for the same purposes of treating articular or incisional pain. However, the secondary reference of Yamahira et al teaches the use of atelocollagen which encompasses type I fibrillar collagen as a carrier for sustained-release of a medicament such as indomethane for about 3 days (72 hours) or 48 hours (See e.g., on col. 5, Experiment 1 and Experiment 2). On col. 3, lines 19-23, the '134 patent states that the ratio of the carrier and the medicament is not critical but, for example, indomethane is preferably incorporated in an amount of 0.0005 to 1 mg per 1 mg of carrier, and interferon is preferably incorporated in an amount of 10^3 to 10^8 IU per 1 mg of carrier. On line 24, the reference continues by stating that one of the characteristics of the present invention is that the preparation can be prepared without using any specific binding agent. Thus, clearly suggesting that ratio of collagen to the pharmaceutical agent is not critical and the

collagen used is non-crosslinked (i.e., no binding agent or crosslinking agent is used). On col. the reference further suggests that the preparation may be incorporated with local anesthetic agents for the intended purposes of treating joints which may includes articular surgery. Further, the reference of Maeda et al teaches the use of collagen which is type I atelopeptide collagen from the skin of bovine as a biodegradable drug carrier (See e.g., abstract, pages 314 and 323). Furthermore, the abstract of Batyrov et al clearly shows the use of collagen as carrier of local anesthetics such as trimecaine in which the collagen prolonged the effect of the local anesthetic. The reference of Solanki et al on page 46 discusses the advantages and disadvantages of using bupivacaine. The expected benefits of bupivacaine, an amide local anesthetic drug, is a popular choice for intraarticular anesthesia, postoperative pain relief, and arthroscopic surgery because of its long-half life.

The prior does not disclose the specific duration time of controlled release formulation, the ratio of collagen to pharmaceutical agent, the amount or the percentages of type I collagen and the concentration of collagen and pharmaceutical agent as claimed. However, the ranges disclosed in the prior art and claimed by Applicant overlap in scope, and as such it is conventional and within the skill of the art to optimize or select the specifics from the ranges disclosed. See *Ex parte Lee*, 31 USPQ2d 1105 (Bd. Pat. App. & inter. 1993); also, See MPEP 2131.03. Further, as acknowledged by Applicant on page 22, lines 25 to page 23, line 5, one of skill in the art would know to adjust the amount of the composition administered, and therefore the amount of pharmaceutical agent delivered, depending on the type of surgical procedure

performed, the site of the procedure and the severity or duration of pain or discomfort likely or usually associated with the procedure performed, as well as the pain tolerance of the patient and the particular composition being administered.

Thus, in view of the above, one of ordinary skill in the art would have been motivated at the time the invention was made to apply the teachings of the secondary references of Yamahira et al (i.e., the duration time of controlled release formulation and the ratio of collagen to the pharmaceutical agent); Maeda et al (use of type I atelopeptide collagen as biodegradable drug carrier); Batyrov et al (use of collagen as a carrier for prolonging the effect of local anesthetic; and Solanki et al (use of anesthetic such as bupivacaine for postoperative pain relief and arthroscopic surgery) to the primary reference of Pavelka et al which teaches the use of a formulation/composition comprising a commercially available Neu Visc™, a viscoelastic dispersion of Type I of highly purified fibrillar atelopeptide collagen containing or including 0.3% anesthetics such as lidocaine for reducing pain in osteoarthritis patients because such features of using collagen as a carrier for prolonging the effect of local anesthetic with controlled release formulation are known or suggested in the art, as seen in the secondary references, and including such features of using the sustained release preparation into the formulations/compositions of the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

Therefore, the combined teachings of the prior art makes obvious the claimed invention's composition/formulation for the treatment of post-surgical articular or

incisional pain or discomfort consisting essentially of an aqueous dispersion of insoluble non-crosslinked type I fibrillar atelopeptide collagen and a pharmaceutical agent which is anesthetic such as bupivacaine or lidocaine, wherein the composition/formulation is formulated to release an effective amount of the pharmaceutical agent from the collagen for at least 48 hours or 72 hours, absent of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDENCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272 0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM

October 12, 2004